About Interbrand Wood Healthcare:

For the past thirty years Interbrand Wood Healthcare has developed specialized services to address the brand challenges faced by the healthcare industry. We have consistently encouraged healthcare clients to view trademark creation as a core component of a global brand and communications strategy. In 1990, rxmark was created as a distinct division of Interbrand Wood to address the growing importance of brand-related research in healthcare. Today, we are widely recognized as a leader in the global assessment of proposed trademarks through proprietary research tools such as the 10/10® Trademark Evaluation Model. Identifying brand names that minimize the potential for harmful medication errors is a top priority of the evaluations we conduct. To date, over 135 trademarks introduced to the marketplace have been first assessed through 10/10® prior to FDA and/or EMEA agency submission, with many more presently awaiting introduction. These 135+ trademarks represent over 1,000 10/10® studies where thousands of proposed pharmaceutical trademarks were evaluated by Interbrand Wood. After nearly 20 years of conducting brand name evaluations Interbrand Wood has learned many significant lessons and would like to offer comments/recommendations regarding the proposed concept paper and pilot program.

General Comments:

We agree with the FDA's position that there is no single fail-safe method or "gold standard" to evaluate proprietary name candidates and that it is necessary for sponsors to employ multiple methods to identify potentially unsafe names. From a macro view, the proposed approach mirrors and builds upon best practices historically employed by our 10/10® Model. 10/10® uses rigorous, multi-faceted research methodologies to aid in the trademark selection process and to identify names that could increase the potential for medication errors, including: quantitative prescription simulation exercises, quantitative closed/open ended surveying techniques, automated/human drug database searches and evaluation/consultation by a multidisciplinary team of dispensing experts.

However, prior to finalizing the concept paper and guidelines for the pilot program it is critical that the FDA consider the current practices healthcare companies partake in to develop viable brand name candidates. Given the present legal/trademark attrition rates, the unpredictable nature of brand name decisions stemming from the regulatory authorities and the desire for "global trademarks" healthcare companies often develop hundreds of candidates for a single compound. In addition, after comprehensive and expensive legal searches are completed in global trademark

databases ten to twenty brand name candidates are typically evaluated in a single name safety study, not just the one or two that are eventually submitted to FDA.

The methods proposed in the concept paper have many practical and logistical implications given the industry dynamic described above. With the current parameters outlined in the concept paper, name validation studies will certainly become more complex and expensive for pharmaceutical companies to execute. The proposed study designs involve implementing multiple research methodologies that will likely require a larger pool of study participants to meet minimum statistical thresholds in comparison to current industry best practices. For example, the FDA has proposed a minimum requirement of 20 prescribing scenarios as part of the prescription simulation exercises. After convening a group of our most senior statisticians within our analytics team, we found that the optimal sample size (defined as one that balances a standard error rate of 5% with a reasonable research budget) will be 400-500 respondents given the FDA's proposed requirements for the prescription simulations. In contrast, our current best practice is to conduct fewer prescription simulations with ~150-200 US healthcare professionals (depending on the compound in question). Combined with other more stringent research requirements such as conducting the promotional review on a per name basis separately from the safety review healthcare companies can expect to see large cost increases for this research. Going forward, it is imperative to identify surveying techniques and study methods that do not detract from the guiding principle of designing a research model that will help us to make an informed decision regarding name safety while also balancing some of these more practical considerations.

As discussed in the concept paper, medication use errors occur due to drug name similarity, unclear labels and/or poorly designed packaging. However, the bigger issue that remains is that we are still not totally certain where the trademark itself falls within the medication error paradigm. As noted at the June 2003 Public Meeting, many participants offered views that prescription and order simulations should reflect actual situations whenever possible. As an industry we must ensure the process we settle on takes into account the entire prescribing and dispensing environment and with some of the methods proposed, including the guidance for the FMEA, we are on the right track. However, even the robust research methods outlined in the concept paper may not simulate the true prescribing /dispensing environment for a proprietary name under consideration. A specialized panel within the Interbrand Wood analytics group tasked with evaluating the proposed pilot program recommends that we also continue to look at new, forward looking surveying techniques and technologies that will help to create more of a "real world" environment for name safety studies.

We hope that standardized methods and endpoints eventually ratified by the FDA will lead to greater predictability and transparency in proprietary name reviews. Sponsors should have a better idea of what the FDA is looking for when conducting proprietary name reviews with the release of the concept paper, which is certainly very helpful and could reduce the current rejection rate. We also believe that the introduction of the concept paper and pilot program will heighten awareness and education around issues related to medication error within the industry. Ultimately though, the goal of the program must be to define consistent standards for acceptability and to create a threshold for approvable names. Unfortunately the process as outlined still requires that certain judgments be made, which will impact our ability to predict a successful outcome. Perhaps it is impossible to fully remove subjectivity from the name review process. However, as stated in the concept paper, it is critical to remain open to new approaches for evaluating trademarks and for us to continue to identify methods that can be replicated and where key research endpoints can be clearly defined. One of the major challenges voiced by many industry participants at the June 2008 public meeting is that despite putting a proposed trademark through this more in-depth and costly evaluation, a company still may not be able to predict a favorable outcome, in terms of the ultimate approval of the name. This lack of incentive is a logistical challenge that the FDA must consider as it tries to encourage companies to participate in the program.

Comments – Safety Review:

- *Preliminary Screening:* We agree with the FDA's proposal to screen brand name candidates for obvious safety conflicts as outlined in the concept paper. This is a common best practice in the name safety assessments we conduct and it is very helpful to have specific guidance from the agency regarding these issues.
- *USAN Stem Search:* We agree with the FDA's proposal to screen brand name candidates for encoding reserved USAN stems. This is a common best practice in the name safety assessments we conduct. However, we also believe that the FDA should offer some flexibility regarding the encoding of reserved two/three letter stems in brand name candidates (especially when the potential conflict involves reserved infixes).
- *Orthographic and Phonetic Similarities/Computational Methods:* We agree with the FDA's proposed approach. These methods are common practices in the name safety assessments we presently conduct. However, we would like to offer some guidance to the agency and industry regarding the proposed online database searches. There is a learning curve when searching for similar drug names in online databases. While the release of POCA software provides another

tool and standardized methodology to identify drug name similarity issues, best practices for search strategies must be defined for other online drug database screens. For example, within the 10/10® Model Interbrand Wood conducts an automated search of the IMS database that employs an algorithm that implements over 900 search strategies to identify conflicts with similar prefixes, infixes and/or suffixes, visual and/or phonetic similarities and similar letter placements or letter combinations. In the spirit of the concept paper and the efforts of the agency/industry we would be happy to participate or lead a best practices committee in this area.

- *Medication Error Data:* The inclusion of medication error data associated with a proposed product that contains an active ingredient marketed domestically or abroad should only be required if:
    - The active ingredient is marketed abroad under a specific brand name and a sponsor applies for the same brand name in the United States.
    - The proposed brand name for the new product is related to the original active ingredient (a good example is a marketed product that will be included as a component of a future fixed dose combination, i.e. Avandia and Avandamet).

  Sponsors could be required to review and submit historic medication error data to demonstrate why the "related" trademark will not pose equal or greater risk in the marketplace that the original trademark. This scenario should provide a reasonable analogue and should help to inform the analysis of the proposed proprietary name. However, if a sponsor proposes a brand name that is not related to the trademark of the marketed active ingredient in any way, then the medication error data will likely not serve as a strong indicator for future safety risk, as the new trademark will likely face different risk factors than the original faced.
- *Name Simulation Studies:* We agree with the FDA's proposal that certain characteristics of real use conditions should be included as part of the prescription simulation process and that marketed drug names should be included as part of the evaluation. While we also agree that the simulation studies should present the name with the corresponding product characteristics, to limit the number of variables in a study where 10-20 name candidates could be considered the corresponding product characteristics should focus on the most likely prescribing conditions (to simulate what the majority of the actual scripts for the product will look and sound like). We would also recommend testing at least one written and one verbal scenario where the proposed brand name is provided without any corresponding product characteristics. This will allow a sponsor to collect data on what would be a high risk prescribing/dispensing scenario and a key potential failure mode (i.e. the prescribing instructions are not complete; differences in dosage

strength, ROA, regimen, etc. do not help to distinguish the two products). As noted earlier in this paper, we believe the optimal sample size (defined as one that balances a standard error rate of 5% with a reasonable research budget) will be 400-500 respondents given the FDA's proposed requirement of 20 scenarios for the prescription simulations. Inclusion of fewer simulations (which is current industry best practice) would allow for a reduction in this sample size. The follow-up questions proposed in the concept paper are conceptually acceptable, although the FDA should look to standardize the phrasing of the actual questions so results can be compared across studies.

- *FMEA*: Interbrand Wood supports the recommendation that multidisciplinary teams of experts be included as part of the review process and FMEA analysis. However, more guidance needs to be provided by the FDA to industry regarding criteria for selection/panelist qualifications. For example, should we as an industry consider a training and certification program in this area? The last thing that can be allowed to happen is that the FDA rejects a brand name because it does not believe the FMEA experts recruited by a sponsor/vendor are qualified to conduct the evaluation. Interbrand Wood has already gone to great lengths to develop an international panel of dispensing experts and can help the agency/industry to define key criteria for selection. Additionally, the FDA should offer guidance to the industry regarding the study design of the FMEA, the questions that should be asked as part of the evaluation and the different points in the medication system that must be considered. Standardization of the methodologies for the FMEA will increase predictability in the results and will offer sponsors greater confidence in the names that pass an independent FMEA. This is a critical component that must be addressed in the final concept paper. It is clear that the FDA will need to take a more active role with sponsors in setting up the FMEA analysis (perhaps even on a per submission basis at the outset of the pilot program) in order to accelerate the learning curve and increase the probability that the FMEA evaluation is reliable and on par with the agency's current best practices.

Comments – Promotional Review:

Based on the information presented at the June 2008 public meeting, the proposed methodologies for conducting the promotional review as outlined in the draft concept paper are more comprehensive and quantitative than the current standard employed by DDMAC. The FDA should clarify why it is recommending such a comprehensive methodology for industry when its current practices are much more qualitative in nature and rely more on the opinions of experts. If the FDA requires an in-depth promotional evaluation as part of the pilot program then perhaps a parallel,

independent review by DDMAC will not be necessary (unless DDMAC replicates the same quantitative methods ratified in the final concept paper). Furthermore, the potential for conflict would exist should DDMAC find a name unacceptable on promotional grounds in its qualitative assessment after a more comprehensive evaluation conducted by a sponsor determines that the name is acceptable.

As stated earlier in this paper, there are a number of practical issues the FDA should consider when providing guidance on how to conduct a promotional review. Requiring companies to conduct the promotional review on a separate track from the safety review and requiring a different sample for each proposed name will augment research costs and time. The question that must be asked is whether this is truly necessary. In our experience, it is not difficult to identify a name that could have significant promotional concerns through very basic assessment (either through primary/secondary research methods). Perhaps the agency could require industry to conduct a more simplistic assessment of its proposed brand name candidates to identify promotional considerations prior to submission (one that is more in line with what is presently used by DDMAC). Then, sponsors could use the more in-depth methods discussed in the concept paper as a means to resolve disputes regarding the viability of a proposed brand name. For example, if a sponsor submits a brand name candidate and DDMAC finds a problem with the name the sponsor would have the option to conduct an experimental study as outlined in the concept paper to explore the issue in greater depth. This would allow a sponsor to be much more efficient with its limited financial resources and focus its efforts on its most preferred candidates. And, employing a standard methodology should allow for greater predictability and less subjectivity in interpreting the results of the follow-up study.

Please direct questions regarding Interbrand Wood's public comments to:

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